Metabolic Syndrome (ICD9 277.7, AR 40-501 4-26) **September 2005**

AEROMEDICAL CONCERNS: Coronary artery disease (CAD) is the leading cause of permanent suspension from flying duties and premature, non-accidental death in aircrew members, with the major concern for sudden incapacitation in flight. Coronary artery disease is silent and evolves over a lengthy period of time, with clinical symptoms and signs being dramatic, life-threatening, or fatal. Numerous risk factors have been identified and are part of the current overall Cardiovascular Screening Program (CVSP) APL. The goal of the program is to identify those at risk for silent disease and mitigate reversible factors before the presence of disease becomes significant and disqualifying/life-threatening.

Metabolic syndrome is a clustering of cardiovascular risk factors including abdominal obesity, hypertriglyceridemia, low levels of high-density lipoprotein (HDL), high-normal blood pressure to hypertension, and impaired glucose tolerance to diabetes. APL's current exist for each of these individual factors, but none include an assessment of cardiovascular health unless these factors also cause a failure in the CAD Screening via failing one of the CVSP criteria. However, not every case of metabolic syndrome will cause a failure of the CVSP. These missed individuals, while having numerous factors, might not otherwise be assessed and provided preventive advice and care. Research has shown that synergy of these factors in metabolic syndrome (even with an aeromedically acceptable blood pressure) markedly increases the risk for development of cardiovascular disease and type 2 diabetes mellitus. Early identification and management of metabolic syndrome is necessary to reduce the risk of development of potential disqualifying conditions and improve the health and well-being of aviation personnel.

Criteria the diagnosis (3 or more of the 5 listed below) is as follows:

Criteria	Males	Females
Abdominal obesity, measured as waist circumference	> 40 inches	> 35 inches
Plasma triglycerides	≥ 150 mg/dl	
Plasma HDL	< 40 mg/dl	<50 mg/dl
Blood pressure	Systolic ≥ 130 or Diastolic ≥ 85 mm Hg	
Fasting glucose	≥ 110 mg/dl	

DISPOSITION: Metabolic syndrome is disqualifying for initial flight applicants. This parallels the disposition of the individual components. For rated aircrew, metabolic syndrome constitutes a failure of Level 1 in the Cardiovascular Screening Program (CVSP), follows the protocol outlined in that APL, and is annotated as INFORMATION ONLY. No specific waiver is required for metabolic syndrome. However, the individual components may warrant the need for an AMS and waiver request.

INFORMATION REQUIRED: Information required should include a thorough assessment of all of the underlying factors and components, to include documentation of

treatment plan IAW with each of the APL's involved. Hypertensive patients warrant screening for type 2 diabetes mellitus. Abdominal circumference, which is not a normal entry for the FDME, should be included with annotation of the height, weight, and Body Mass Index (BMI).

FOLLOW-UP: Annual follow-up is required to review the overall health and progress of treatment. CVSP APL should be followed for those with a diagnosis of metabolic syndrome. Further follow-up guidelines are specified in the appropriate APL for each of the components of concern.

TREATMENT:

1. **Lifestyle changes**— Lifestyle changes should be the FIRST therapy prescribed unless individual components below warrant therapy as 7-10% weight loss may obviate the need for additional medications initially. Weight loss through exercise (30 minutes/day, 5 days/week) and dietary changes are recommended. Lifestyle modification is the best method for reducing the risk of CAD and progression towards type 2 diabetes. Reducing abdominal obesity decreases insulin resistance and the hyperinsulinemic state, which improves free fatty acid, carbohydrate, and lipoprotein metabolism.
2. **Hypertension/Borderline (JNC VII)**—use of ACE-inhibitor or ARB to reduce BP below 130/85 is recommended. See Hypertension APL.
3. **Hyperlipidemia**—use of Statins, to reduce LDL to < 100 mg/dl and improve HDL and lower triglycerides. Additional use of fibrates (Tricor is preferred over Lopid due to increased risk of side effects) and/or niacin may be needed, but these come with increased concern of side effects. See Hyperlipidemia APL.
4. **Type 2 Diabetes/Impaired Glucose Tolerance**—use of Metformin helps with insulin utilization, reducing hepatic release, and weight reduction. Use of TZD helps with reducing hyperinsulinemia, which helps reverse the dysmetabolism, and preserving beta-cell function. In patients without type 2 diabetes mellitus, these medications do not reduce the risk of development of Coronary Artery Disease. See Diabetes APL—medication use requires AMS and waiver recommendation.
5. **Aspirin**—unless contraindicated, use of enteric-coated aspirin (81 to 325 mg) daily is recommended for all those over 35 years of age.

DISCUSSION: Metabolic syndrome was first described in 1988 and termed Syndrome X. It has been also referred to as dyslipidemic hypertension, atherogenic lipoprotein pattern, and dysmetabolic syndrome X. The formal definition of metabolic syndrome, as published in 2001 from the National Cholesterol Education Program Adult Treatment Panel III guidelines are include three or more positives of the five listed criteria above.

Being on hypertensive OR glucose therapy meets criteria, and being on hyperlipidemic therapy may meet one or both of the lipoprotein criteria.

Metabolic syndrome is thought to be a product of complex pathophysiology involving progressive resistance of peripheral tissues to the effects of plasma insulin with disruption of normal metabolism with free fatty acids (FFA), carbohydrates, and lipoprotein. A synergy occurs with the factors above their independent contribution to accelerate coronary artery disease (CAD). Age, inactivity, and excessive calories worsen this.

NHANES III data (1988-1994) found the prevalence of metabolic syndrome to be 24%, or 47 million, of Americans, with 44% of Americans having 2 or more of the traits. These numbers are increasing with the continued societal problem of obesity and physical inactivity. Metabolic syndrome prevalence increases with age (1 in 16 ages 20-29 versus 1 in 3 ages 50-59 to 4 in 9 ages 60-69) and is seen more in minority populations. While related to insulin resistance syndrome, metabolic syndrome is distinct entity often appearing later on in the process.

Observational data from the Framingham study showed that metabolic syndrome accounted for almost 25% of all new-onset CAD. Although at one time felt to be a better predictor of CAD than the Framingham Risk Score, the additional components of metabolic syndrome have added little to the predictability of CAD risk to date. However, numerous studies have demonstrated the increased risk of CAD, cardiovascular death (CVD), and development of type 2 diabetes mellitus coming from the constellation of factors comprising the metabolic syndrome. Individual studies have shown a 3 to 5-fold increased risk of CAD or CVD and a 7 to 34-fold increased risk of developing type 2 diabetes mellitus. While the ADA and other organizations are currently evaluating metabolic syndrome's role in CAD and diabetes, the clustering is easily identified and warrants regimented follow-up in aviation personnel to improve overall health and well-being.

SELECTED REFERNCES:

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